

U.S. 09/073,596

Reply to Office action of 10 February 2005

**Amendments to Claims:**

This listing of claims will replace all prior versions and listings in the application:

**Listing of Claims:**

- 1-81. (Cancelled)
82. (Withdrawn) An *in vitro* composition comprising an enriched and expanded population of proliferating cell precursors.
83. (Cancelled)
84. (Previously Presented) The composition according to claim 101, wherein the dendritic cell precursors are human.
85. (Withdrawn) The composition of dendritic cell precursors according to claim 84, wherein the dendritic cell precursors are obtained from blood.
86. (Withdrawn) The composition of dendritic cell precursors according to claim 84, wherein the dendritic cell precursors are obtained from bone marrow.
87. (Withdrawn) The composition according to claim 83 wherein the antigen is produced by tumor cells.
88. (Withdrawn) The composition according to claim 83 wherein the antigen is immunoglobulin.
89. (Previously Presented) The composition according to claim 101, wherein the antigen is a microorganism.
90. (Withdrawn) The composition according to claim 83 wherein the antigen is a virus.
91. (Previously Presented) The composition according to claim 89, wherein the antigen is a polypeptide.
92. (Previously Presented) The composition according to claim 89, wherein the antigen is a peptide.
93. (Withdrawn) The composition according to claim 83 wherein the antigen is a self-protein or auto-antigen.
94. (Currently Amended) The composition according to claim 101, wherein the antigen is a ~~mycobacteria~~ mycobacterium.

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95. (Previously Presented) The composition according to claim 94, wherein the mycobacterium is BCG.
96. (Withdrawn) A composition comprising an enriched population of human dendritic cells and a pharmaceutically acceptable carrier.
97. (Cancelled)
98. (Withdrawn) A mixed culture of activated dendritic cells and T cells.
99. (Currently Amended) The pharmaceutical composition according to claim 116, wherein the antigen-activated dendritic cells express an amount of the ~~modified~~ fragmented antigen to provide between about 1 to 100 micrograms of the ~~modified~~ fragmented antigen in said pharmaceutical composition.
100. (Withdrawn) A pharmaceutical composition comprising a dendritic cell modified antigen wherein a substance to be modified is exposed to a culture of isolated dendritic cell precursors and whereby the substance is modified by the dendritic cells to produce modified antigen.
101. (Currently Amended) An *in vitro* composition comprising ~~an enriched and expanded population of~~ antigen-activated dendritic cells presenting ~~modified~~ fragmented antigen derived from an *in vitro* culture of an enriched and expanded population of proliferating dendritic cell precursors by a method comprising:  
providing a tissue source comprising dendritic cell precursors;  
optionally treating the tissue source comprising dendritic cell precursors to increase the proportion of dendritic cell precursors;  
culturing the tissue source on a substrate in a culture medium comprising GM-CSF to obtain cell clusters;  
subculturing the cell clusters to produce cell aggregates comprising proliferating dendritic cell precursors; and  
subculturing the cell aggregates at least one time to enrich the proportion of dendritic cell precursors;  
wherein the dendritic cell precursors are cultured *in vitro* in the presence of an antigen for a time sufficient to allow the antigen to be ~~modified~~ fragmented and presented.

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102. (Withdrawn) The composition of proliferating dendritic cell precursors according to claim 82 further comprising GM-CSF.
103. (Previously Presented) The pharmaceutical composition according to claim 116, wherein the pharmaceutical composition comprises from about  $1 \times 10^6$  to  $1 \times 10^7$  antigen activated dendritic cells.
104. (Previously Presented) The composition according to claim 101, wherein the tissue source is blood.
105. (Previously Presented) The composition according to claim 101, wherein the tissue source is bone marrow.
106. (Previously Presented) The composition according to claim 101, wherein GM-CSF is present in the culture medium at a concentration of about 1-1000 U/ml.
107. (Previously Presented) The composition according to claim 104, wherein the concentration of GM-CSF in the culture medium is about 30-100 U/ml.
108. (Previously Presented) The composition according to claim 105, wherein the concentration of GM-CSF in the culture medium is about 50-1000 U/ml.
109. (Currently Amended) The composition according to claim 101, wherein the cell aggregates are blood derived and are subcultured from about one to five times.
110. (Currently Amended) The composition according to claim 101, wherein the cell aggregates are subcultured ~~about~~ every 3 to 30 days.
111. (Previously Presented) The composition according to claim 101, wherein the claim medium is selected from the group consisting of RPMI 1640, DMEM and  $\alpha$ -MEM, and wherein the culture medium is supplemented with serum.
112. (Previously Presented) The composition according to claim 104, wherein the tissue source is treated to remove red blood cells.
113. (Previously Presented) The composition according to claim 105, wherein the tissue source is treated to remove B cells and granulocytes.
114. (Currently Amended) The composition according to claim 101, wherein said antigen is presented by the dendritic cells on MHC class I or MHC class II molecules.
115. (Currently Amended) The composition according to claim 101, wherein said ~~modified~~ fragmented antigen is presented by the dendritic cells on MHC class I or MHC class II molecules.

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116. (Previously Presented) A pharmaceutical composition comprising a therapeutically effective amount of the composition according to claim 101.
117. (Previously Presented) The composition according to claim 94, wherein the mycobacterium is a tuberculosis bacteria.
118. (Previously Presented) The composition according to claim 101, wherein the dendritic cell precursors are cultured in the presence of antigen for between 1-48 hours.
119. (Previously Presented) The composition according to claim 118, wherein the dendritic cell precursors are cultured in the presence of antigen for about 20 hours.
120. (Currently Amended) An *in vitro* composition comprising ~~an enriched and expanded population of~~ antigen-activated dendritic cells, wherein said antigen-activated dendritic cells are derived from an *in vitro* culture of a population of enriched and expanded proliferating precursor cells which were contacted *in vitro* with antigen in the presence of GM-CSF for a sufficient time for antigen ~~modification~~ fragmentation and presentation to occur.
121. (New) The composition of claim 101, wherein the cell aggregates are serially subcultured one to five times.